## REMARKS

### Introductory Comments

Claims 1, 3, 5-7, 11-14 and 19-21 were examined in the Office Action under reply and stand rejected under (1) 35 U.S.C. §112, first paragraph (claims 1-3, 5-7, 11-14 and 19-21); (2) 35 U.S.C. §102 (1, 2, 5, 6, 19 and 21); and (3) 35 U.S.C. §103(a) (claims claims 1-3, 5-7 and 11-14). These rejections are traversed and believed to be overcome for reasons discussed below. Applicants note with appreciation the withdrawal of the previous rejections under 35 U.S.C. §112, second paragraph.

### Overview of the Above Amendments

Claims 1-3, 5-7 and 11-14 have been cancelled and claims 19 and 21 have been amended to recite the invention with greater particularity. Specifically, claims 19 and 21 now recite that the vector particle is "an FIV vector particle" produced from "an FIV vector" comprising a 5' "FIV LTR" and a 3' "FIV LTR." Support for these amendments can be found in the claims as filed, as well as throughout the specification at e.g., page 18, lines 17-20.

The above amendments are made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled subject matter.

### Formal Matters

The Office states: "The amendment filed December 2, 2004 is redundant and does not amend the claims relative to the prior version of the claims." However, as clearly stated on the RCE request, the amendment provided with the request was a duplicate **copy** of the amendment and supporting evidence filed on June 14, 2004. The copy was provided for the Examiner's convenience. Applicants apologize for any confusion this may have caused.

**Rejections Under 35 U.S.C. §112, First Paragraph**

The Office rejected all pending claims under 35 U.S.C. §112, first paragraph as nonenabled. With respect to pending claims 19-21, the Office argues the claims are directed only to *in vivo* methods and "the specification fails to adequately teach how to use the claimed methods therapeutically." Office Action, page 3. In particular, the Office argues "expression of β-galactosidase does not constitute a therapeutic effect" and that β-galactosidase "is clearly not indicative that a gene delivery system can provide a therapeutic benefit as evidenced by the high level of failure in gene therapy clinical trials which were preceded by successful expression of β-galactosidase in animal studies." Office Action, pages 3-4. The Office cites Ross et al., *Hum. Gene Ther.* (1996) 7:1781-1790 ("Ross") in support of this argument. However, Ross published almost four years prior to the filing date of applicants' priority application and therefore does not reflect the state of the art at the time the application was filed. The field of gene therapy had advanced tremendously over that period of time.

The Office also continues to cite Rubanyi et al., *Molec. Aspects Med.* (2001) 22:113-142 ("Rubanyi") as representing the state of the art at the time the application was filed. However, applicants submit Rubanyi actually evidences the feasibility of gene therapy techniques. As of Rubanyi's publication date, there were 368 gene therapy clinical protocols or trials in progress world wide (see, pages 125-126 of Rubanyi), evidencing that this procedure is indeed viewed as legitimate and useful. The fact that **ALL** gene therapy methods are not ultimately found useful does not provide a proper basis for a rejection under 35 U.S.C. §112, first paragraph. The notion that one of ordinary skill in the art must have reasonable assurances of obtaining positive results on every occasion has been emphatically rejected. *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976). Thus, the fact that the claims might encompass inoperative embodiments is not a proper basis for rejection. See, e.g., MPEP §2164.08(b); and *In re Angstadt*, at p. 219. So long as it is clear that some embodiments render the claims operative, the inclusion of possible inoperative species cannot invalidate the claim under 35 U.S.C. §112, first paragraph. See, also, *In re Cook*, 169 USPQ 298 (CCPA 1971); *Horton v.*

*Stevens*, 7 USPQ2d 1245, 1247 (Fed. Cir. 1988).

As previously explained to the Examiner, applicants have described and are claiming a gene delivery system that indeed provides for efficient expression of the gene contained within the vector in cerebellar neurons. The Examiner, however, argues that applicants have taught only β-galactosidase expression and that one of skill in the art would not expect β-galactosidase expression to have a therapeutic effect. However, applicants have indeed taught more than just β-galactosidase expression. Applicants throughout the specification detail methods for delivering a large number of genes encoding therapeutic proteins for use in treating a wide variety of CNS and cerebellar diseases. There is absolutely no requirement for examples. Applicants have enabled a gene delivery system and have shown that this system indeed provides for efficient transduction and expression. Applicants have shown this using β-galactosidase, a marker routinely relied on by scientists in the discipline of gene therapy as predictive of whether a particular gene delivery system can provide a therapeutic benefit when used to deliver a therapeutic gene of interest.

To evidence that the β-galactosidase gene is routinely used to study transgene delivery and expression and is indeed predictive of a therapeutic benefit, applicants previously provided a number of papers and abstracts from well-respected, peer-reviewed journals. The Examiner disputes this evidence, arguing these papers only show that gene therapy has a "promise" or "potential" for being useful. However, there are many, many examples of gene therapy protocols that indeed turned out to be successful after first testing delivery of the gene with β-galactosidase. Moreover, applicants provided evidence that (1) therapeutic proteins could successfully be delivered and expressed in the cerebellum using their vector system (see, e.g., Haskell et al., *Gene Ther.* (2003) 10:34-42); and (2) that a therapeutic benefit could in fact be achieved using their vector system (see, e.g., Brooks et al., *Proc. Natl. Acad. Sci.* (2002) 99:6216-6221). The Examiner disputes these assertions, arguing Haskell pertains to a gene not described in applicants' specification and Brooks did not show expression in cerebellar neurons. However, just because TPP-1 was not mentioned in applicants' specification does not mean the

evidence provided is not credible. Moreover, as explained above, applicants have shown successful delivery and expression in cerebellar neurons. Contrary to the Examiner's assertions, applicants have indeed taught how to make and use the invention and have therefore satisfied the enablement requirement of 35 U.S.C. §112, first paragraph.

Notwithstanding the above, applicants are submitting the Declaration of Beverly L. Davidson, Ph.D. Dr. Davidson is renowned in the field of gene therapy, having authored or coauthored approximately 380 publications! See, the copy of Dr. Davidson's CV that accompanies her Declaration. As explained in paragraph 3 of the Declaration, it is routine in the field of gene therapy to first deliver a reporter gene such as β-galactosidase in order to determine whether successful delivery and expression of a therapeutic gene is even feasible. It is Dr. Davison's belief that successful delivery and expression of β-galactosidase is in fact a predictor that a therapeutic protein could be delivered and expressed with a subsequent therapeutic effect. This view is widely accepted in the field of gene therapy. Moreover, Dr. Davidson explains in paragraph 6 of the Declaration that she "would expect that lentivirus-mediated gene delivery of therapeutic proteins, such as β-glucuronidase, would also be successful in providing expression in cerebellar neurons with a therapeutic effect." In fact, it is Dr. Davidson's opinion that "there is every reason to believe that expression of a therapeutic protein in cerebellar neurons can result in a therapeutic benefit, such as treating or preventing a CNS disorder, and treating or preventing cerebellar degeneration." See, paragraph 7 of the Declaration.

Should the Examiner maintain the rejections in light of Dr. Davidson's Declaration, applicants request the Examiner provide her qualifications as one of skill in the art of gene therapy by a declaration pursuant to 37 CFR §1.104(d)(2).

Based on at least the foregoing arguments, applicants respectfully request the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

**Rejections Over the Art**

Claims 1, 2, 5, 6, 19 and 21 stand rejected under 35 U.S.C. §102, as anticipated by Bosch et al., *Hum. Gene Ther.* (2000) 11:1139-1150 ("Bosch"). Bosch is said to "disclose the use of an HIV-1 vector for gene delivery to the cerebellum in an animal model of lysosomal storage disease." Office Action, page 9. However, applicants respectfully submit the claims are not anticipated by Bosch.

In order to be anticipatory, a single reference must disclose each and every element of the claims. *See, e.g., Hybritech v. Monoclonal Antibodies,* 231 USPQ 81 (Fed. Cir. 1986). Moreover, the single source must disclose all of the claimed elements arranged as in the claims. *See, e.g., Richardson v. Suzuki Motor Co.,* 9 USPQ2d 1913 (Fed. Cir. 1989). Bosch fails to disclose each and every element of applicants' claimed invention and therefore does not anticipate applicants' claims.

In particular, all of the pending claims are directed to the use of an FIV vector. Bosch in no way pertains to methods using FIV vector particles. The Examiner appears to recognize this as none of the claims reciting FIV vector particles were subject to this rejection. Accordingly, this basis for rejection has been overcome and withdrawal thereof is respectfully requested.

Claims 1-3, 5-7 and 11-14 were rejected under 35 U.S.C. §103(a) as being unpatentable over Poeschla et al., *Nature Med.* (1998) 4:354-357; Dow et al., *J. Acquired Immune Def. Synd.* (1990) 3:658-668 ("Dow"); and Cummings et al., *Nat. Genet.* (1998) 19:148-154 ("Cummings"), as well as over Curran et al., *Molec. Ther.* (2000) 1:31-38 and Dow and Cummings. Solely in an effort to advance prosecution, all of the rejected claims have been cancelled. Thus, these bases for rejection have been overcome and withdrawal thereof is respectfully requested.

## CONCLUSION

Applicants respectfully submit that the claims define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested. If the Examiner notes any further matters which she believes may be resolved by a telephone interview, she is encouraged to contact the undersigned attorney at (650) 493-3400.

Respectfully submitted,

Date: 6/27/05

By: _____

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